A translational viewpoint explaining its potential salutary effects

de Leeuw, Anne E; de Boer, Rudolf A

Published in:
European Heart Journal. Cardiovascular Pharmacotherapy

DOI:
10.1093/ehjcvp/pvw015

Publication date:
2016

European Heart Journal – Cardiovascular Pharmacotherapy (2016) **2**, 257
doi:10.1093/ehjcvp/pvw015

A translational viewpoint explaining its potential salutary effects

Dear Editor,

We thank Dr Martinez-Martin *et al.* for their interest in our article.[1] In their letter, the authors question if 'SGLT1 has no compensatory role during the inhibition of SGLT2'. We referred to a study published by Gembardt *et al.*[2] in diabetic *ob/ob* mice with complete pharmacological blockade of SGLT2. In contrast to the study published by Rieg *et al.*,[3] Gembardt did not report an upregulation of renal SGLT1 protein levels and differential results on the levels of SGLT1 mRNA in *ob/ob* diabetic mice under complete SGLT2 blockade. But the observed (incomplete) 30–50% inhibition of reabsorption by SGLT2 inhibitors appears to be the sum of SGLT1 compensation and residual SGLT2 activity.[4] So, we agree with the authors of the letter that our wording is overstated and thank them for pointing this out.

With respect to the second comment about Table 1, we aimed to review the most important effects of SGLT2 inhibition, and due to space constraints, we had to limit ourselves to effects to key organs. It is correct that SGLT2 is also expressed outside of organs mentioned by (i.e. kidney, brain, thyroid, and heart); we realize that the full list of all organs that express SGLT2 contains >20 organs.[5]

We thank the readers Martinez-Martin, Jimenez-Martin, and Sablon-Gonzalez for their awareness and suggestions.

References

1. de Leeuw AE, de Boer RA. SGLT2 inhibition: cardioprotection by treating diabetes. A translational viewpoint explaining its potential salutary effects. *Eur Heart J Cardiovasc Pharmacother* 2016;**2**:244–255.
2. Gembardt F *et al.* The SGLT2 inhibitor empagliflozin ameliorates early features of diabetic nephropathy in BTBR ob/ob type 2 diabetic mice with and without hypertension. *Am J Physiol Ren Physiol* 2014;**307**: F317–F325.
3. Rieg T *et al.* Increase in SGLT1-mediated transport explains renal glucose reabsorption during genetic and pharmacological SGLT2 inhibition in euglycemia. *Am J Physiol Ren Physiol* 2014;**306**:F188–F193.
4. Lu Y, Griffen SC, Boulton DW, Leil TA. Use of systems pharmacology modeling to elucidate the operating characteristics of SGLT1 and SGLT2 in renal glucose reabsorption in humans. *Front Pharmacol* 2014;**5**:274.
5. http://www.genecards.org/cgi-bin/carddisp.pl?gene=SLC2A2&keywords=SGLT2 (16 May 2016).

Anne E. de Leeuw and Rudolf A. de Boer*
University Medical Center Groningen (UMCG), Department of Cardiology, University of Groningen,
AB43, Hanzeplein 1, 9713GZ
Groningen, The Netherlands

*Corresponding author. Tel: +31 50 361 5340, Fax: +31 50 361 5525, Email: r.a.de.boer@umcg.nl